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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,583	11/28/2000	Christiaan M. Saris	MBHB00-1213	9474

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EXAMINER
MERTZ, PREMA MARIA

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/724,583	Applicant(s) Saris et al.
	Examiner Prema Mertz	Art Unit 1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 2, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-8, 10, 11, and 42-46* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-8, 10, 11, and 42-46* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 9, 12-41, 47-56 have been canceled in Paper No. 10, ½/03. Claims 4-8, 42-44, and amended claims 1-3, 10-11, 45-46 (Paper No. 10, ½/03), are under consideration.

2. Receipt of applicant's arguments and amendments filed in Paper No. 10 (½/03) is acknowledged.

3. The following previous rejections and objections are withdrawn in light of applicants amendments filed in Paper No. 10, ½/03:

(i) the objection to the title of the invention;

(ii) the rejection of claims 12, 4-8, 10-12, 42-46 under 35 U.S.C. § 112, first paragraph for the deposit requirement.

4. Applicant's arguments filed in Paper No. 10 (½/03), have been fully considered but were deemed persuasive in part. The issues remaining, are stated below.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim rejections-35 USC § 112, first paragraph

6. Claims 2-8, 10-11, 42-46 are rejected under 35 U.S.C. 112, first paragraph.

This rejection is maintained for reasons of record set forth at pages 7-11 of the previous Office action (Paper No. 8, 7/2/02).

Applicants argue that they have amended claim 2 to recite a fragment of the polypeptide of SEQ ID NO:2 that has activity. However, the issue here is the breadth of the claims in light of the

predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. This position is consistent with the decisions in In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) and Amgen Inc. V. Chugai Pharmaceuticals Co. Ltd., 13 USPQ2d, 1737 (1990), and In re Wands, 8USPQ2d, 1400 (CAFC 1988) (which has been cited by Applicants. If Applicants will kindly review page 1404 of In re Wands, they will find that the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims. Applicants arguments that the standard is that of mutating a nucleic acid encoding a subject protein and testing to see if it retains the desired biological activity is a position that has been routinely dismissed by the courts, as shown by the decisions cited above.

Further, In re Wands determined that the repetition of work which was disclosed in a patent application as producing a composition containing an antibody, which is a naturally-occurring compound, did not constitute undue experimentation even if the antibody produced thereby was not identical to those that were disclosed in that application. The instant claims are not limited to naturally-occurring compounds and the instant specification does not provide a description of a repeatable process of producing a nucleic acid encoding a fragment of SEQ ID NO:2 or a nucleic acid encoding a polypeptide with at least one modification that is a conservative amino acid substitution,

C-terminal truncation or N-terminal truncation of SEQ ID NO:2. Recitation of "a nucleic acid encoding a polypeptide with at least one modification that is a conservative amino acid substitution" encompasses nucleic acids in which every single amino acid has been changed to produce a polypeptide with a completely disparate amino acid sequence in contrast to SEQ ID NO:2. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is d described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of those amino acid residues of the disclosed naturally-occurring sequence, which are required for functional and structural integrity of the protein. It is this additional characterization of the disclosed protein that is required in order to obtain the functional and structural data needed to permit one to produce a protein which meets both the structural and functional requirements of the instant claims that constitutes undue experimentation.

Furthermore, Applicant is encouraged to review the discussion of 35 U.S.C. § 112, first paragraph, in a recent CAFC decision, Genentech, Inc. v. Novo. Nordisk, 42 USPQ2d, 100 (CAFC 1997), in which the decisions in In re Fisher, Amgen Inc. V. Chugai Pharmaceuticals Co. Ltd., and In re Wands were considered as the controlling precedents in determining enablement issues where protein and recombinant DNA issues are concerned. These decisions have been relied upon in the instant rejection and by the Court because they show that the judicial interpretation of the first paragraph of 35 U.S.C. § 112 requires that the breadth of claims must be based upon the predictability of the claimed subject matter and not on some standard of trial and error. To argue that

one can make material embodiments of the invention and then test for those that work in the manner disclosed or that the instant claims only encompass the working embodiments is judicially unsound. Unless one has a reasonable expectation that any one material embodiment of the claimed invention would be more likely than not to function in the manner disclosed or the instant specification provides sufficient guidance to permit one to identify those embodiments which are more likely to work than not, without actually making and testing them, then the instant application does not support the breadth of the claims. In the instant case it is highly improbable that a nucleic acid encoding a fragment of SEQ ID NO:2 or a nucleic acid encoding a polypeptide with at least one modification that is a conservative amino acid substitution, C-terminal truncation or N-terminal truncation of SEQ ID NO:2 will more likely than not perform in the manner disclosed and the instant specification does not provide the guidance needed to predictably alter either of the sequences with any reasonable expectation that the resulting protein will have the desired activity.

The cited portion of the specification (Table I, pages 27-28) merely outlines residues which are considered conservative. This is not adequate guidance as to the nature of the nucleic acid analogues or variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Furthermore, the claim does not indicate the number of conservative substitutions i.e. there is no upper limit to the amount of substitutions. Therefore Applicants have not presented enablement commensurate in scope with the claims.

Claim rejections-35 U.S.C. 112, second paragraph

7. Claims 1-8, 10-11, 42-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is maintained for reasons of record set forth at pages 11-13 of the previous Office action (Paper No. 8, 7/2/02).

Applicants argue that claims 1-3 have been amended to recite "hybridizes under at least moderately stringent conditions" and the claims as amended are not indefinite. However, contrary to Applicants arguments, the claims as amended are still vague and indefinite. The specification on page 23, lines 17-24, recites an example of a typical "moderately stringent condition." Therefore, since the conditions recited in the specification are exemplary, the stringent condition claimed is a relative and conditional term and renders the claims indefinite. The metes and bounds of the claims thus cannot be ascertained.

Applicants argue that with respect to claims 2-3 which recite the phrase "has an activity of the polypeptide set forth in SEQ ID NO:2", only those nucleic acid molecules encoding IL-1ra-R polypeptide variants that possess an inherent activity of the polypeptide as set forth in SEQ ID NO:2 are encompassed by the claims. However, contrary to Applicants arguments, the issue here is that it is unclear which "activity" of those described in Example 9 on page 119 and those which have yet to be discovered are encompassed by the instant claims.

Applicants argue that claim 46 has been amended to recite "biologically-active fragment", however, contrary to Applicants arguments, the claim is still vague and indefinite because the metes

and bounds of the term fragment are unclear. A single amino acid comprises a "biologically-active fragment".

Claim Rejections - 35 USC § 102

8a. Claims 1-8, 10-11, 42-46, are rejected under 35 U.S.C. 102(a) as being anticipated by WO 9937662 (1999).

This rejection is maintained for reasons of record set forth at pages 13-14 of the previous Office action (Paper No. 8, 7/2/02).

Applicants argue that the cDNA disclosed in the reference shares a sequence identity of only 32.4% with the nucleotide sequence of SEQ ID NO:1 and in view of the specification's teaching that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79% (page 23, lines 23-24), it is apparent that the cDNA disclosed in the reference would not hybridize to the nucleotide sequence of SEQ ID NO:1 under Applicants' recited stringency conditions. However, contrary to Applicants arguments, the conditions recited in the specification, page 23, lines 21-24, are exemplary and recites "about a 21% mismatch" by way of example. Furthermore, Applicants argue that the protein encoded by the cDNA of the reference will not possess the inherent activity of the IL-1ra-R polypeptide set forth in SEQ ID NO:2. However, contrary to Applicants arguments, the claims do not recite any activity for the protein encoded by the nucleic acid that hybridizes to the nucleic acid of SEQ ID NO:1. For all the reasons recited above, the cDNA disclosed in the reference meets the limitations of the claimed invention.

8b. Claims 1-8, 10-11, 42-46 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 855 404 A1 (1998).

This rejection is maintained for reasons of record set forth at pages 14-15 of the previous Office action (Paper No. 8, 7/2/02).

Applicants argue that the cDNA disclosed in the reference shares a sequence identity of only 50.9% with the nucleotide sequence of SEQ ID NO:1 and in view of the specification's teaching that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79% (page 23, lines 23-24), it is apparent that the cDNA disclosed in the reference would not hybridize to the nucleotide sequence of SEQ ID NO:1 under Applicants' recited stringency conditions. However, contrary to Applicants arguments, the conditions recited in the specification, page 23, lines 21-24, are exemplary and recites "about a 21% mismatch" by way of example. Furthermore, Applicants argue that the protein encoded by the cDNA of the reference will not possess the inherent activity of the IL-1ra-R polypeptide set forth in SEQ ID NO:2. However, contrary to Applicants arguments, the claims do not recite any activity for the protein encoded by the nucleic acid that hybridizes to the nucleic acid of SEQ ID NO:1. For all the reasons recited above, the cDNA disclosed in the reference meets the limitations of the claimed invention.

8c. Claims 1-8, 10, 42 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,075,222 (1991).

This rejection is maintained for reasons of record set forth at page 15 of the previous Office action (Paper No. 8, 7/2/02).

Applicants argue that the cDNA disclosed in the reference shares a sequence identity of only 28.8% with the nucleotide sequence of SEQ ID NO:1 and in view of the specification's teaching that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79% (page 23, lines 23-24), it is apparent that the cDNA disclosed in the reference would not hybridize to the nucleotide sequence of SEQ ID NO:1 under Applicants' recited stringency conditions. However, contrary to Applicants arguments, the conditions recited in the specification, page 23, lines 21-24, are exemplary and recites "about a 21% mismatch" by way of example. Furthermore, Applicants argue that the protein encoded by the cDNA of the reference will not possess the inherent activity of the IL-1ra-R polypeptide set forth in SEQ ID NO:2. However, contrary to Applicants arguments, the claims do not recite any activity for the protein encoded by the nucleic acid that hybridizes to the nucleic acid of SEQ ID NO:1. For all the reasons recited above, the cDNA disclosed in the reference meets the limitations of the claimed invention.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the

date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (703) 308-4229. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 305-3014 or (703 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 746-5300.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
January 29, 2003